

Probiotics in the prevention of traveller's diarrhoea

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TRAVELLER'S DIARRHOEA

Every year millions of people travel from the industrialized countries to the developing countries. Traveller's Diarrhoea (TD) is a common syndrome affecting healthy travellers not only in developing countries but also in Europe. The incidence of TD ranges from 20 to 50% depending on the origin and the destination of the traveller as well as the mode of travel (1,2). TD is defined as the passage of ≥ 3 unformed stools in a 24 h period and although it is often self-limiting, there is a considerable morbidity (3,4).

Approximately 3% of international travellers to high-risk areas develop persistent diarrhoea. By definition the duration of persistent diarrhoea is at least 14 days, but it may last several months to a year. In approximately 50% of travellers with persistent diarrhoea, it lasts more than 30 days (5). However, even when the diarrhoea is self-limiting, minor attacks can interrupt a holiday, causing inconvenience and discomfort (1).

CAUSING AGENTS

Traveller's diarrhoea is often caused by the intake contaminated foods or beverages (6).

Various infectious agents have been described as the cause of TD. Enterotoxigenic *Escherichia coli* (ETEC) is the most commonly isolated organism (1,2). It is estimated that up to 40% of cases of TD are due to these ETEC bacteria (6). Another 40% of cases are caused by bacterial infections with *Shigella* spp., *Salmonella* spp. and *Campylobacter jejuni* (3). Being careful with food and water is therefore the number one precaution. However, it does not seem to be enough to prevent TD in all cases.

TREATMENT OF TD

Antibiotic prophylaxis has proved to be effective and shorten the duration of the TD episode (6). However, economic, safety and microbiological considerations discourage its widespread use (7). Especially the growing problem of antibiotic resistance and the possibility of adverse effects from antimicrobial agents weigh strongly against recommending antibiotic prophylaxis routinely (6).

Since even small attacks of traveller's diarrhoea can interrupt a holiday, the travelling public has great interest in safe, cost-effective alternative treatments or, even better, means to prevent TD (2,4).

The prevention of traveller's diarrhoea by probiotics could be a

safe alternative to antibacterial drugs; probiotics have shown to have a beneficial effect in some studies performed with travellers. A few examples will be described below (1,8).

PROBIOTICS

Probiotics can be defined as non-pathogenic micro-organisms that, when ingested, exert a positive influence on the health or physiology of the host. Probiotics consist of either yeast or bacteria, especially lactic acid bacteria. Their fate in the gastrointestinal tract and their effects differ among strains.

The effects of probiotics can be direct through modulation of the endogenous microflora or indirect through modulation of the immune system. Many health claims have been made concerning probiotics, especially concerning their potential to prevent or help cure intestinal disturbances (4).

A wide variety of probiotics have been used to treat or as prophylaxis against traveller's diarrhoea with varying results. Among the probiotics used are *Lactobacillus rhamnosus* GG (LGG), *Lactobacillus acidophilus*, *Bifidobacterium bifidum*, *Streptococcus thermophilus* and *Saccharomyces boulardii*. In only a few studies combinations of strains are used.

PROBIOTICS AND TRAVELLER'S DIARRHOEA

Many studies have investigated the efficacy of LGG in preventing traveller's diarrhoea. In one, 820 travellers to two resorts in Turkey failed to show an overall effect of the use of LGG as preventative, as 43% of the controls and 38% of the treatment group developed diarrhoea. However, when the data from one resort was examined separately, the difference in diarrhoea was 40% for controls and 24% for the treatment group, which was significant (9). In a second study with 245 travellers to varying destinations in developing countries, the risk of diarrhoea on any given day was 3.9% in travellers that took *Lactobacillus* GG and 7.4% in control subjects that took a placebo (8).

In a study with Austrian travellers, *Saccharomyces boulardii* was used as a potential protective agent against TD. The protection against the occurrence of diarrhoea was mild but significant and was dose-dependent (4).

The above mentioned studies offer encouraging results, but in another study with Austrian tourists, no effect was found for *Lactobacillus acidophilus* or *Enterococcus faecium* (9).

In only one study so far probiotics have proven to be really effective. In this study a combination of strains was used; *Lactobacillus acidophilus*, *Bifidobacterium bifidum*, *Lactobacillus bulgaricus* and *Streptococcus thermophilus*. Probiotic capsules

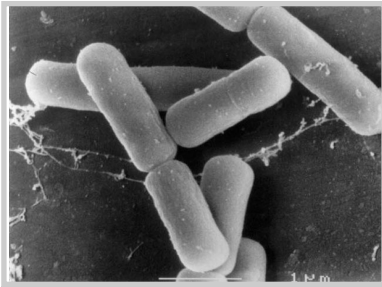


Foto 1
Lactobacilli

were administered to 195 Danish tourists on a 2-week trip to Egypt (3). The frequency of traveller's diarrhoea was significantly reduced from 71% in the placebo group to 43% in the group that received the probiotic (4).

DIFFICULTIES IN CLINICAL STUDIES

Other studies have been performed, also with varying results. Differences in populations involved and the probiotic strains used, a lack of aetiological data and difficulties in monitoring compliance have been suggested as being responsible for these inconclusive results (10). Further studies are clearly needed to verify this effect in different populations and travel destinations (11).

The above mentioned studies highlight the mechanistic problems associated with prophylactic trials on the effects of probiotics against TD, not least because TD is caused by a diverse, ever-changing range of microbial pathogens, including pathogenic *E.coli*, *Salmonella*, *Shigella* and *Campylobacter* strains as well as viruses. It is therefore unlikely that a single probiotic strain will inhibit such a broad spectrum of pathogens

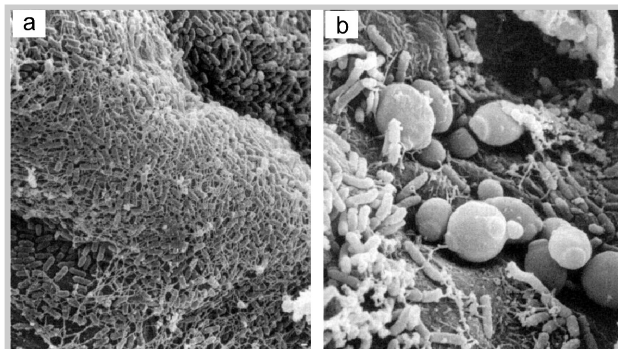


Foto 2
Healthy (a) and unhealthy (b) flora

in vivo (12). This is confirmed by the fact that the best results are found in a study in which a combination of four probiotic strains was used.

CONCLUSIONS

Probiotics are very promising in preventing travellers to foreign countries from diarrhoea or other intestinal problems. However, not every probiotic strain or product seems to be effective. From the above it can be concluded that multispecies probiotics are more effective than probiotics with only one strain. To develop a product for the prevention of traveller's diarrhoea, one should look at the specific characteristics that the probiotic bacteria need to be effective; for example the inhibition of pathogens (ETEC) or adhesion to the intestinal cells. Besides specific criteria, the product should meet some general criteria like a good shelf-life and survival through the gastro-intestinal tract. A probiotic concept has recently been developed, containing seven different probiotic strains selected for their properties based on the above mentioned criteria.

REFERENCES

1. Gismondo MR, Drago L, Lombardi A. 1999. Review of probiotics available to modify gastrointestinal flora. *International Journal of Antimicrobial Agents*, 12; 287-292.
2. Rolfe RD. 2000. The role of probiotic cultures in the control of gastrointestinal health. *Journal of Nutrition*, 130; 396S-402S.
3. McNaught CE, MacFie J. 2001. Probiotics in clinical practice: a critical review of the evidence. *Nutrition Research*, 21; 343-353.
4. Marteau PR, De Vrese M, Cellier CJ, Schrezenmeir J. 2001. Protection from gastrointestinal diseases with the use of probiotics. *American Journal of Clinical Nutrition*, 73 (Suppl.); 430S-436S.
5. Schultz C. 1999. *Escherichia coli* and persistent diarrhoea. Thesis; Academic Medical Centre, University of Amsterdam.
6. Nataro JP, Kaper JB. 1998. Diarrheagenic *Escherichia coli*. *Clinical Microbiology Reviews*, 11 (1); 142-201.
7. Castelli F, Beltrame A, Carosi G. 1998. Principes et pratiques du traitement ambulatoire de la "tourista". 3ème Journéebiennale de Médecine des Voyages.
8. De Roos NM, Katan MB. 2000. Effects of probiotic bacteria on diarrhea, lipid metabolism, and carcinogenesis: a review of papers published between 1988 and 1998. *American Journal of Clinical Nutrition*, 71; 405-411.
9. Teitelbaum JE, Walker WA. 2002. Nutritional impact of pre- and probiotics as protective gastrointestinal organisms. *Annual Reviews Nutrition*, 22; 107-138.
10. Gill HS. 2003. Probiotics to enhance anti-infective defences in the gastrointestinal tract. *Best Practice & Research Clinical Gastroenterology*, 17 (5); 755-773.
11. Saarela M, Lähteenmäki L, Crittenden R, Salminen S, Mattila-Sandholm T. 2002. Gut bacteria and health foods – the European perspective. *International Journal of Food Microbiology*, 78; 99-117.
12. Tuohy KM, Probert HM, Smejkal CW, Gibson GR. 2003. Using probiotics and prebiotics to improve gut health. *DDT*, 8 (15); 692-700.